REMARKS

This application, as amended herein, maintains claims 50 – 118, and newly added claim 119.

Applicant thanks the Examiner for the indication of allowability of claims 51, 54, 55, 59 - 66, 68-80, 86, 87, 89, 92, 93 and 95 – 115. However, in view of the amendments and remarks submitted herein, it is respectfully submitted that all of claims 50 - 119 are directed to patentable subject matter.

Claims 50 and 82 were rejected as anticipated by Wang et al. This rejection is respectfully traversed.

Claim 50 has been amended herein to recite:

A method for calculating digital calibration filters for a Mass Spectrometry (MS) instrument system, comprising the step of:

obtaining, from a given calibration ion with its isotopes, at least one actual mass spectral peak shape function,

specifying mass spectral target peak shape functions within respective mass spectral ranges, and

performing a deconvolution operation between the obtained at least one mass spectral peak shape function and the mass spectral target peak shape functions to obtain at least one digital calibration filter from a result of the deconvolution operation.

Thus, claim 50, as amended above clearly requires obtaining, from a given calibration ion with its isotopes, at least one actual mass spectral peak shape function and obtaining at least one digital calibration filter. In view of this amendment, it is clear that Wang et al does not anticipate or render obvious claim 50, for the following reasons.

First, it is clear that Wang et al. do not teach anything concerning obtaining, from a given calibration ion with its isotopes, at least one actual mass spectral peak shape function. In fact there is absolutely no mention of the word "ion" or "isotope" in Wang et al., while ions and isotopes are the cores of mass spectrometry. Second, Wang et al. teaches approximate, idealized, and theoretical peak shape functions in optical spectroscopy (Col. 6 lines 10-36 on calculating theoretical peak shape functions based on rectangles from eqn 1, Col. 7 line 19 on idealized peak shape functions, Col. 7 line 24 to "approximate" actual peak shape functions, Col 8 lines 15-16 and eqns. 1-2 on rectangular peak shape functions theoretically proportional to wavenumbers), not actual peak shape functions. Third, Wang et al. teaches optical filters installed on a filter wheel, and at best a transformation filter between two different instruments. The transformation filter is directed to theoretical, not actual, optical spectra peak shapes (see, in addition to the above citations, Wang et al., at col. 3, lines 17 – 26, and lines 38-43). Fourth, Wang et al does not teach or suggest performing a deconvolution operation between the obtained at least one mass spectral peak shape function and the mass spectral target peak shape functions to obtain at least one digital calibration filter from a result of the deconvolution operation.

It is noted that the Examiner has relied on Wang et al. for teachings with respect to mass spectra. However, Wang et al. merely speculates with respect to mass spectrometry (column 11, lines 6-9), but really has nothing whatsoever to do with mass spectrometry. Wang et al. deals with standardization between different instruments which produce optical spectra, such as that produced in a Fourier Transform Infrared Instrument (FTIR). In fact, a word search of Wang et al. reveals that Wang et al. only mentions the words "mass spectrometers" at the single place cited above as an afterthought, and there is absolutely no teaching of how to apply what is taught in Wang et al. to mass spectrometry. Further, the problems of optical instruments such as an FTIR instrument, are vastly different than those of mass spectrometry. Optical spectroscopy deals with analyzing light associated with a sample. It has nothing whatsoever to do with the complex problems associated with a mass spectrometer of ionizing a sample, separating the ions with its isotopes in accordance with mass to charge ratio, detecting the ions, and

determining the abundance of the various species in accordance with mass to charge ratio. It is thus respectfully submitted that Wang et al. does not anticipate claim 50 and is not a proper reference to use to reject the claims, which are directed to methods and apparatus of mass spectrometry. The Examiner is simply wrong in asserting throughout the action that Wang et al. disclose mass spectral peak shape functions, because Wang et al. simply teach no such thing.

In fact, it is respectfully submitted that every citation to Wang et al by the Examiner is simply not applicable to clam 50. For example, column 4, lines 65-66 describe an optical system with optical fibers and optical filters on a rotating filter wheel, and not a digital calibration filter. Column 8, lines 60-65 describe conventional wavenumber calibration for an optical system, and have nothing to do with peak shape, and certainly nothing to do with mass spectral peak shape. With specific reference to the citation to column 8, lines 12-32, it is pointed out that lines 15-16 and eqns. 1-2 specifically state that the peak shape functions used in Wang et al. are theoretically derived to be proportional to wavenumber, not actual ones based on measurements. Other such examples could be cited. Further, it is respectfully pointed out that such citations by the Examiner should be reconsidered in light of the amended claims presented herein.

In view of the above, it is submitted that claim 50 is directed to patentable subject matter.

Claim 82 has been amended in a manner precisely analogous to the amendment of claim 50. For precisely the same reasons set forth above with respect to claim 50, including why the citations by the Examiner are not applicable, claim 82 is also directed to patentable subject matter.

The exact nature of the rejection of claims 53, 56, 57, 58, 67, 81, 83, 84 and 85 is not stated in the office action, as the paragraphs referring to these claims are under the paragraph referring to claims 50 and 82. However, as will be demonstrated by the examples below, not one of the portions of Wang et al. referred to by the Examiner teaches or suggests mass spectral data or peak shape functions of any kind.

With specific reference to claim 53, Wang et al. do not even mention the word "interpolation". The reference by the Examiner to Fig. 1 and col. 4, lines 65-66 of Wang et al. is simply not understood.

With reference to claim 56, the Fourier transform mentioned in column 6, lines 10-43 of Wang et al. refers to converting a time domain interferogram into a frequency domain spectrum. However, the Fourier deconvolution of claim 56 involves division of Fourier components which Wang et al. simply do not address in any way. The same is true with respect to the reference to column 6, lines 18-43, in the rejection of claim 57.

With reference to the rejection of claim 58, it is pointed out that the references to portions of Wang et al. are simply not correct. First, as noted above, a full text search of Wang et al. does not come up with any of the words "interpolation" or "interpolating" or "interpolate" anywhere in the text. Further, since theoretical peak shapes are used, Wang et al. do not need to perform any interpolation as the peak shapes can be theoretically calculated wherever desired, with possibly large errors compared to actual peak shapes (as set forth in claim 50, from which claim 58 depends).

With reference to claim 67, and col. 7, lines 4-65 of Wang et al. it is pointed out that Wang et al. teaches only one transformation, with absolutely no reference to pre-calibration or post-calibration transformations.

With regard to the cited portion of Wang et al. relied upon by the Examiner to reject claim 81, it is pointed out that Fig. 3 of Wang et al. shows the operation of two instruments with respect to a same or other sample, with no reference to standards or mixing of the standards into a sample. The text section does not mention the mixing of any standards into a test sample. A text search of Wang et al. for "infusion" or "mixing" yields no results. Thus the reference to col. 7, line 4 to col. 8, line 11 of Wang et al. is simply irrelevant.

With regard to claims 83, 84 and 85, it has already been pointed out that there is absolutely no reference to interpolation in Wang et al. With specific reference to claim 85, Wang et al. do discuss weights, but there is no regression involved. The words "regression" or "regress" do not appear at any point throughout the text of Wang et al.

Thus, for all of the reasons set forth above, and for all of the reasons set forth with respect to claims 50 and 82, it is submitted that claims 53, 56, 57, 58, 67, 81, 83, 84 and 85 are all directed to patentable subject matter.

Claims 52 and 88 were rejected as obvious over Wang et al. in view of Rather. This rejection is respectfully traversed.

Claims 52 and 88, as amended herein, state calculating, <u>for a given calibration ion,</u> relative isotope abundances and theoretical mass locations of isotopes corresponding to the at least one mass spectral peak and performing convolution operations on <u>both</u> calculated relative isotope abundances and measured isotope peak clusters using a <u>same continuous function with a narrow peak width</u>. Rather clearly does not teach or suggest using a same continuous function with narrow peak width on both. Further, for the reasons stated above, Wang et al. certainly do not suggest this. Claims 52 and 88, as amended herein, also recite performing a deconvolution operation between the measured isotope peak clusters and calculated isotope peak clusters after said convolution operations to obtain the at least one actual mass spectral peak shape function <u>in the presence of mutually interfering isotopes</u>. Support for this amendment may be found in the specification at page 6, lines 5-12. Neither Wang et al. nor Rather teach or suggest claims 52 or claim 88, whether taken alone or in combination.

Still further, the sections of Wang et al. cited by the Examiner, refer to how to calculate a theoretical peak shape function (not how to obtain actual peak shape function), one that is theoretical and proportional to the wavenumber, and a conventional wavenumber calibration that does not involve peak shape function. In this rejection, the citation by the Examiner to Wang et al. teaches the details of how to approximate (col. 5, line 62 to col.

6, line 10) peak shape functions through theoretically derived equations, and <u>not</u> how to obtain actual peak shape functions. While there are occasions on which the symbol "/" may represent deconvolution, no deconvolution operation is carried out in Wang et al. The "/" in eqn. 1 and in col. 6, line 33 of Wang et al. are straight divisions, not deconvolutions.

Thus, Wang et al. is not relevant for the reasons set forth above, and for the reasons set forth with respect to claims 50 and 82. Rather adds nothing significant to the teachings of Wang et al. that is relevant with respect to claims 52 and 88.

Specifically, Rather does not obtain actual peak shape function. In fact, Rather teaches away form Applicant's invention, as set forth in claims 52 and 88. In this regard, reference is made to page 4, paragraph 0029 of Rather, wherein it is stated that:

> With this procedure; the peak width of the time-of-flight signals does not become part of the peaks in the composite histogram spectrum (as with histograms by TDCs) but the measured peak intensities are maintained so that the correct isotope distributions are measured even if higher ion currents exist which result in a large number of ions in a peak in a single spectrum.

Further, page 6, paragraph 0047 of Rather states that:

> The algorithm should calculate both the position, i.e the time of flight, and the intensity of the peak. The position is best found by a smoothed calculation of the first derivative, where the zero crossover with successively calculated derivative values indicates a maximum (or minimum) value in each case. The direction of the zero crossover indicates whether it is a maximum or minimum. The intensity is calculated by a summation via the main component of the peak.

Finally, paragraph 0065 of Rather, which was specifically relied upon by the Examiner, states:

> FIG. 4 shows a measurement curve which has been acquired using the method according to the invention. An ADC with a clock time of 2 MHz was used but an averaged time of flight for the ions of the associated ion signal and an averaged intensity were determined from each individual spectrum. (emphasis added).

Thus, actual peak shape function is not obtained or preserved in the teachings of Rather.

Even if Wang et al. and Rather are combined, they do not anticipate or render obvious performing convolution operations on both calculated relative isotope abundances and measured isotope peak clusters using a same continuous function with a narrow peak width, a key step of the invention defined in claims 52 and 88, and as stated in the specification on page 19, lines 15-17.

In summary, in Rather, there is no application of a same continuous function with a narrow peak width to both the calculated relative isotope abundances and measured isotope peak clusters. Rather does not obtain actual peak shape functions. Rather does not utilize the actual peak shape functions for mass spectral calibration.

Since Wang et al., for the reasons set forth above is simply not relevant, it is improper to make the combination of Wang et al. and Rather in the first place, and even if the combination or references is made, claims 52 and 88 are not obvious over the references. Thus, it is respectfully submitted that the rejection of claims 52 and 88, for which the Examiner must rely on a combination of unrelated and deficient references, is simply not tenable. Withdrawal of the rejection of claims 52 and 88 is respectfully requested.

The remaining claims that were rejected depend from one of the independent claims discussed above. These claims have further recitations, which in combination with the

recitations of the claim from which they depend, are not taught or suggested in the art of record.

With specific reference to claims 90, 91, 94 and 119-118, the references by the Examiner to portions of Wang et al. simply do not refer to mass spectral peak shape function, or to mass spectroscopy at all. Further, as discussed above the specific portions of Wang et al. relied upon by the Examiner do not refer to Fourier deconvolution, actual (as opposed to theoretical) peak shapes, interpolation, or the mixing of samples. What has happen here is that the Examiner, in rejecting the claims, is impermissibly bootstrapping a passing conjecture concerning mass spectroscopy, when there is no teaching concerning how to apply anything in Wang et al. to the field of mass spectroscopy. As pointed out above, the technological considerations concerning dealing with ions and isotopes are vastly different than those for dealing with light, which is what Wang et al teaches. Thus, it is submitted that claims 90, 91, 94 and 119-118 are also directed to patentable subject matter.

In summary, as pointed out by the Examiner, Wang et al. failed to teach isotope abundances and theoretical mass locations of the isotopes, calculated relative isotope abundances and measured isotope peak clusters using a same continuous function with a narrow peak width. Rather does deal with ions and isotopes as they pertain to mass spectrometry, but did not perform convolution operation involving both the calculated relative isotope abundances and measured isotope peak clusters, and certainly does not mention using a same continuous function with a narrow peak width. Rather does not teach operations to obtain at least one mass spectral peak shape function. Wang et al. did not teach operations to obtain at least one actual mass spectral peak shape functions in the presence of mutually interfering isotopes (see specification, page 6, lines 5-12 of the present application), as now reflected in the amended claims. Thus, claims 52, 88, 90, 91, 94 and 119-118 are all directed to patentable subject matter.

Newly added claim 119 states that the digital filter, when applied to a mass spectrum performs at least one of noise filtering, signal averaging, mass calibration, and peak shape

adjustment. Support for claim 119 may be found in the specification at page 25, lines 1-2; page 39, lines 12-13; page 41, lines 12-14 and in Figs. 10B & 10C. Claim 119 is also directed to patentable subject matter.

Conclusion

For all of the reasons set forth above, it is respectfully submitted that this application is in a condition for allowance. However, if there are any issues that remain that can be resolved by telephone, the Applicant and the undersigned respectfully request that the Examiner telephone the undersigned with a view toward working together to resolve those issues, and to allow this application to proceed to grant.

Please charge deposit account no. 502244 in the amount of $50 for the additional claim fee due with this paper, for the presentation of one new dependent claim that refers to two other claims. If any additional fee is required, please charge deposit account no. 502244. A duplicate of this last page is enclosed.

Respectfully submitted,

David Aker

7/13/2005
Date

David Aker, Reg. No. 29,277
23 Southern Road
Hartsdale, NY 10530
Tel. & Fax 914 674-1094

SERIAL NO.: 10/689,313 FILED: 10/20/2003